

What is claimed is:

1. A method of treating or ameliorating an autoimmune disorder or an inflammatory disorder or one or more symptoms thereof, said method comprising
5 administering to a subject in need thereof a dose of a therapeutically effective amount of one or more CD2 binding molecules, wherein administration of said dose results in CD2 binding molecules binding to at least 25% of the CD2 polypeptides expressed by peripheral blood lymphocytes.
- 10 2. A method of treating or ameliorating an autoimmune disorder or an inflammatory disorder or one or more symptoms thereof, said method comprising administering to a subject in need thereof a dose of a therapeutically effective amount of one or more CD2 binding molecules, wherein administration of said dose results in a mean
absolute lymphocyte count of approximately 500 cells/ μ l to below 1200 cells/ μ l.
- 15 3. A method of treating or ameliorating an autoimmune disorder or an inflammatory disorder or one or more symptoms thereof, said method comprising administering to a subject in need thereof a dose of a therapeutically effective amount of one or more CD2 binding molecules, wherein administration of said dose results in an
20 approximately 25% or more reduction in said subject's mean absolute lymphocyte count relative to said subject's mean absolute lymphocyte count prior to the administration of said dose.
- 25 4. The method of claim 2 further comprising administering to said subject one or more subsequent doses of a therapeutically effective amount of one or more CD2 binding molecules after administration of said first dose, wherein administration of said subsequent doses maintain a mean absolute lymphocyte count of approximately 500 cells/ μ l to below 1200 cells/ μ l.
- 30 5. The method of claim 2 further comprising administering to said subject one or more subsequent doses of a therapeutically effective amount of one or more CD2 binding molecules after administration of said first dose, wherein administration of said subsequent doses maintain an approximately 25% or more reduction in said subject's absolute mean lymphocyte count relative to said subject's mean absolute lymphocyte count prior to the
35 administration of said first dose.

6. The method of claim 4, wherein said subsequent dose is administered at least 1 week after the administration of said first dose.

7. The method of claim 1 further comprising administering to said subject one or more subsequent doses of a therapeutically effective amount of one or more CD2 binding molecules after administration of said first dose, wherein said administration of said subsequent doses restore at least 25% of the CD2 polypeptides expressed by peripheral blood lymphocytes being bound by CD2 binding molecules.

8. The method of claim 1 or 3, wherein said dose results in CD2 binding molecules binding to at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75% or at least 80% of the CD2 polypeptides expressed by peripheral blood lymphocytes for at least 1 hour after the administration of said dose and prior to the administration of a subsequent dose.

9. The method of claim 7, wherein said first dose results in CD2 binding molecules binding to at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75% or at least 80% of the CD2 polypeptides expressed by peripheral blood lymphocytes.

10. The method of claim 7, wherein said first dose results in a mean absolute lymphocyte count of approximately 500 cells/ μ l to below 1200 cells/ μ l and said subsequent doses restore a mean absolute lymphocyte count of approximately 500 cells/ μ l to below 1200 cells/ μ l.

11. The method of claim 3 or 9, wherein a subsequent dose is administered when the percentage of CD2 polypeptides bound to CD2 binding molecules drops to 20% or less, 15% or less, or 10% or less.

12. The method of claim 3 or 9, wherein a subsequent dose is administered when the mean absolute lymphocyte count increases to approximately 1250 cells/ μ l or more.

13. A method of treating or ameliorating an autoimmune disorder or an inflammatory disorder or one or more symptoms thereof, said method comprising administering to a subject in need thereof a dose of a therapeutically effective amount of

one or more CD2 binding molecules and administering to said subject one or more subsequent doses of a therapeutically effective amount of one or more CD2 binding molecules after administering a prior dose, wherein said CD2 binding molecules do not inhibit the interaction between LFA-3 and CD2.

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14. The method of claim 1, 2 or 3, wherein said CD2 binding molecules are not small organic molecules.

15. A method of treating or ameliorating an autoimmune disorder or an
10 inflammatory disorder or one or more symptoms thereof, said method comprising:

- (a) administering to a subject in need thereof one or more doses of a therapeutically effective amount of one or more CD2 binding molecules;
- (b) monitoring the mean absolute lymphocyte count in said subject after the administration of one or more of said doses and prior to the administration of
15 a subsequent dose; and
- (c) maintaining a mean absolute lymphocyte count of approximately 500 cells/ μ l to below 1200 cells/ μ l by repeating step (a) as necessary.

16. A method of treating or ameliorating an autoimmune disorder or an
20 inflammatory disorder or one or more symptoms thereof, said method comprising:

- (a) administering to a subject in need thereof one or more doses of a therapeutically effective amount of one or more CD2 binding molecules;
- (b) monitoring the mean absolute lymphocyte count of said subject after the administration of one or more of said doses and prior to the administration of
25 a subsequent dose; and
- (c) maintaining a mean absolute lymphocyte count in said subject of 25% less than the mean absolute lymphocyte count in said subject prior to the administration of said doses of therapeutically effective amounts of one or more CD2 binding molecules by repeating step (a) as necessary.

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17. A method of treating or ameliorating an autoimmune disorder or an
inflammatory disorder or one or more symptoms thereof, said method comprising:

- (a) administering to a subject in need thereof one or more doses of a therapeutically effective amount of one or more CD2 binding molecules; and

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- (b) monitoring the mean absolute lymphocyte count in said subject after administration of a certain number of doses and prior to the administration of a subsequent dose.

5 18. The method of claim 17, wherein the certain number of doses is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12 doses.

 19. The method of claim 18 further comprising administering one or more subsequent doses of a therapeutically effective amount of one or more CD2 binding
10 molecules based upon whether the lymphocyte count is within the range of approximately 500 cells/ μ l to 1200 cells/ μ l.

 20. A method of treating or ameliorating an autoimmune disorder or an inflammatory disorder or one or more symptoms thereof, said method comprising:
15 (a) administering to a subject in need thereof one or more doses of a therapeutically effective amount of one or more CD2 binding molecules;
 (b) assessing the percentage of CD2 polypeptides bound by CD2 binding molecules after administration of one or more of said doses and prior to the administration of a subsequent dose; and
20 (c) administering to said subject one or more subsequent doses of a therapeutically effective amount of one or more CD2 binding molecules when the percentage of CD2 polypeptides expressed by peripheral blood lymphocytes bound by CD2 binding molecules is approximately 20% or less.

25 21. A method of treating or ameliorating an autoimmune disorder or an inflammatory disorder or one or more symptoms thereof, said method comprising:
 (a) administering to a subject in need thereof one or more doses of a therapeutically effective amount of one or more CD2 binding molecules;
 (b) monitoring the percentage of CD2 polypeptides bound by CD2 binding
30 molecules after administration of one or more of said doses and prior to the administration of a subsequent dose; and
 (c) maintaining at least a 25% receptor occupancy by said CD2 binding molecules in said subject by repeating step (a) as necessary.

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22. A method of treating or ameliorating an autoimmune disorder or an inflammatory disorder or one or more symptoms thereof, said method comprising:

- (a) administering to a subject in need thereof one or more doses of a therapeutically effective amount of one or more CD2 binding molecules; and
- (b) monitoring the percentage of CD2 polypeptides expressed by peripheral blood lymphocytes bound by CD2 binding molecules in said subject after administration of a certain number of doses and prior to the administration of a subsequent dose.

23. The method of claim 22, wherein the certain number of doses is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12 doses.

24. A method of treating or ameliorating psoriasis or one or more symptoms thereof, said method comprising administering to a subject in need thereof one or more doses of a therapeutically effective amount of one or more CD2 binding molecules, wherein administration of said doses results in a mean absolute lymphocyte count of approximately 500 cells/ μ l to below 1200 cells/ μ l.

25. A method of treating or ameliorating psoriasis or one or more symptoms thereof, said method comprising administering to a subject in need thereof one or more doses of a therapeutically effective amount of one or more CD2 binding molecules, wherein administration of said doses results in at least 25% of CD2 polypeptides expressed by peripheral blood lymphocytes being bound by CD2 binding molecules.

26. The method of claim 25, wherein said doses result in CD2 binding molecules binding to at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75% or at least 80% of the CD2 polypeptides expressed by peripheral blood lymphocytes.

27. A method of treating or ameliorating psoriasis or one or more symptoms thereof, said method comprising administering to a subject in need thereof one or more doses of a therapeutically effective amount of MEDI-507.

28. The method of claim 27, wherein administration of said doses results in a lymphocyte count of approximately 500 cells/ μ l to below 1200 cells/ μ l.

29. The method of claim 27, wherein administration of said doses results in at least 30% of CD2 polypeptides expressed by peripheral blood lymphocytes being bound by MEDI-507.

5 30. The method of claim 29, wherein said doses result in at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75% or at least 80% of the CD2 polypeptides expressed by peripheral blood lymphocytes being bound by MEDI-507.

10 31. The method of claim 24, 25, 26, 27 or 28, wherein at least a 25% reduction of said subject's Psoriasis Area and Severity Index (PASI) score is achieved.

32. The method of claim 31, wherein the PASI score is reduced by at least 50%.

15 33. The method of claim 31, wherein the PASI score is reduced by at least 75%.

34. A method of treating or ameliorating psoriasis in a human which method reduces or avoids adverse effects associated with decreasing lymphocyte counts, said method comprising administering doses of a therapeutically effective amount of one or
20 more CD2 binding molecules, said doses being effective to achieve a reduction in said human's PASI score by at least 25% but insufficient to cause a reduction in lymphocyte count to below 500 cells/ μ l.

35. The method of claim 34, wherein at least a 50% reduction in said human's
25 PASI score is achieved.

36. The method of claim 34, wherein the lymphocyte count is between 500 cells/ μ l and 1200 cells/ μ l.

30 37. The method as in any one of claims 1-5, 13, 17 and 22, wherein the autoimmune disorder is rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, Reiter's Syndrome, systemic lupus erythematosus, dermatomyositis, Sjogren's syndrome, lupus erythematosus, multiple sclerosis, or myasthenia gravis.

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38. The method as in any one of claims 1-5, 13, 17 and 22, wherein the inflammatory disorder is asthma, encephalitis, inflammatory bowel disease, chronic obstructive pulmonary disease (COPD), arthritis, or an allergic disorder.

5 39. The method as in any one of claims 1-5, 13, 17 and 22, wherein the autoimmune disorder is characterized by increased infiltration of lymphocytes into affected dermal or epidermal tissues.

40. The method as in any one of claims 1-5, 13, 17 and 22, wherein the autoimmune disorder is characterized by increased T cell activation or abnormal antigen
10 presentation.

41. The method as in any one of claims 1-5, 13, 17 and 22, wherein the autoimmune disorder is psoriasis.

15 42. The method of claim 41, wherein the psoriasis is chronic plaque psoriasis.

43. The method of claim 1, 2, 3 or 13, wherein said dose is administered parenterally.

20 44. The method of claim 27, 28 or 29, wherein said doses of MEDI-507 are administered parenterally.

45. The method as in any one of claims 1-5, 13, 17, 22, and 24, wherein at least one of the CD2 binding molecules is a fusion protein.

25 46. The method as in any one of claims 1-5, 13, 17, 22, and 24, wherein at least one of the CD2 binding molecules is an antibody.

47. The method of claim 46, wherein the antibody is LO-CD2a/BTI-322 or an
30 antigen-binding fragment thereof.

48. The method of claim 46, wherein the antibody is a human or humanized monoclonal antibody.

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49. The method of claim 46, wherein the antibody is MEDI-507 or an antigen-binding fragment thereof.

50. The method as in any one of claims 1-5, 13, 17, 22, 24, and 27-29, wherein
5 said effective amount is a dose of approximately 150 µg/kg or less, approximately 125
µg/kg or less, approximately 100 µg/kg or less, approximately 75 µg/kg or less,
approximately 50 µg/kg or less, approximately 40 µg/kg or less, approximately 30 µg/kg or
less, approximately 20 µg/kg or less, approximately 10 µg/kg or less, approximately 5
µg/kg or less, approximately 2 µg/kg or less, approximately 1 µg/kg or less, or
10 approximately 0.5 µg/kg or less.

51. The method as in any one of claims 1-5, 13, 17, 22, 24, and 27-29, wherein
said effective amount is a dose of between approximately 0.05 µg/kg and 150 µg/kg.

52. The method as in any one of claims 1-5, 13, 17, 22, 24, and 27-29, wherein
15 the subject is a human subject.

53. The method of claim 4, 5, or 7, wherein the first dose is administered
parenterally.
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54. The method of claim 4, 5, or 7, wherein the subsequent doses are
administered parenterally.

55. The method of claim 1, 2, 3 or 13, wherein said dose is administered
25 subcutaneously.

56. The method of claim 27, 28 or 29, wherein said doses of MEDI-507 are
administered subcutaneously.

57. The method of claim 4, 5, or 7, wherein the first dose is administered
30 subcutaneously.

58. The method of claim 4, 5, or 7, wherein the subsequent doses are
administered subcutaneously.
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59. An article of manufacture comprising packaging material and a pharmaceutical agent contained within said packaging material, wherein said pharmaceutical agent comprises a CD2 binding molecule and a pharmaceutically acceptable carrier,

5 wherein said article of manufacture includes instruction means indicating a dosing regimen comprising administering an initial dosing, and optionally administering a subsequent dose or doses, of said pharmaceutical agent to a subject suffering from one or more symptoms associated with an autoimmune disorder or an inflammatory disorder,

wherein the instruction means suggests a dosing regimen comprising an initial
10 dosing that results in CD2 binding molecules binding to at least 30% of the CD2 polypeptides expressed by the subject's peripheral blood lymphocytes for at least 1 hour after the administration of said initial dosing, and

wherein the instruction means suggests a dosing interval for said dosing regimen such that any dose/doses administered subsequent to said initial dosing, if administered,
15 is/are only administered when 20% or less of the CD2 polypeptides expressed by peripheral blood lymphocytes are bound by previously administered CD2 binding molecules.

60. An article of manufacture comprising packaging material and a pharmaceutical composition in suitable form for administration to a human contained within
20 said packaging material, wherein said pharmaceutical composition comprises MEDI-507 or an antigen-binding fragment thereof, and a pharmaceutically acceptable carrier.

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